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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/905,709	08/05/97	STERN D	52876/JPW/JM

EXAMINER	
LAZAR-WESLEY,E	
ART UNIT	**PAPER NUMBER**
1646	5

HM11/1001

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NEW YORK NY 10036

DATE MAILED: 10/01/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-35 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-35 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

Specification

1. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

2. The attempt to incorporate subject matter into this application by reference to Schmidt et al., 1992, Neeper et al., 1992 , Schmidt et al., 1994 is improper because the structure of the soluble receptor for advanced glycation end product is considered essential material.

Applicants are reminded that, if they wish to incorporate sequence disclosures, they have to comply with the requirements of 37 CFR 1.821-1.825.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-35 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The structure of the soluble receptor for advanced glycation end product, that is critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). This rejection might be overcome by a proper incorporation by reference as discussed above. However, issues of scope enablement might arise concerning any /all soluble receptor for advanced glycation product.

5. Claims 1-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for "a polypeptide derived from soluble receptor for advanced glycation end product". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. While the Examiner takes note of the discussion on derivative, page 8, line 31 through page 9, line 8, the term derivative encompasses chemical modication, mutated forms, conjugates, etc..., and it is unpredictable which molecule would be functional. In view of the lack of guidance and of working example, it would constitute undue experimentation for one of skill in the art to make and/or use the invention commensurate in scope with the claims.

The specification is not enabling "to prevent accelerated atherosclerosis in a subject predisposed thereto", or "to prevent a macrovessel disease in a subject predisposed thereto". The specification discloses examples (page 32, line 33, page 34, line 25) of treatment of diabetic mice with sRAGE, but the specification is not enabled for prevention of the diseases, because it does not provide guidance about how to determine who is predisposed to the diseases or at which stage of the disease the polypeptide should be administered. In view of the lack of guidance and working example, and as it is unpredictable who is predisposed to the disease and when the preventive treatment should be applied, it would constitute undue experimentation to make and/or use the invention commensurate in scope with the claims.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite, because it recites a "polypeptide derived from soluble receptor for advanced glycation product", without providing the metes and bounds of what is encompassed by "derived". Such term might for example encompass mutated forms, chemical modifications, conjugates, cross-linked forms, etc...

Claims 10and 27 are indefinite because they recite "at least a portion of", and it is not clear what else should be present in the polypeptide besides a portion of the soluble receptor.

Claims 12, 13, 29, 30 are indefinite because they do not define the structure or the metes and bounds of the polypeptide considered. Furthermore, claims 13 and 30 read on any dipeptide from " the naturally occurring soluble receptor for advanced glycation product", and it is unlikely that any such dipeptide would be functional.

Claim 34 lacks antecedent basis for "the sRAGE".

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neeper e tal., J.Biol.Chem. 267(1):14998-15004, July 25, 1992, in view of Schmidt et al., Artheriosclerosis and Thrombosis 14(10): 1521-1528, cited by applicants, and Bernton , US Patent 5,605,885(A).

Neeper et al. Teach the cloning and expression of a cell surface receptor for advanced glycosylation end product (Figure 3) and defines the structural domain of the receptor (page 15000, col.2 first paragraph). He teaches also that other AGE binding proteins have been disclosed (page 15003, col.2, second full paragraph).

He does not teach a method of prevention using the soluble receptor.

Schmidt et al. Teach a link between the accumulation of AGEs in the vessel wall and the accelerated vascular disease that occurrs during the course of diabetes (page 1521, col.2, last 5 lines).

Bernton et al.(A) teach the use of a soluble prolactin receptor to bind to and neutralize the prolactin in order to antagonize the effect of prolactin (col.4, lines 25-40).

It would have been obvious for one of skill in the art at the time of the invention , to use a soluble receptor for AGE in order to bind with high affinity and neutralize AGEs, therefore preventing the accumulation of AGEs in the vessel wall and the accelerated vascular disease. One would have had reasonable expectation of success in view of Bernton's teachings.

As for the claim limitations concerning the choice of subject to be treated, the choice of fragment of the soluble receptor, the doses and methods of administration, they constitute obvious modifications for one of skill in the art.

10. Claims 1-35 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Wautier et al., J.Clin.Invest.97(1):238-243, January 1996, cited by applicants.

Wautier teaches that the soluble receptor for advanced glycation end product blocks hyperpermeability in diabetic rats (page 242, col.1. He teaches that increased vascular permeability is characteristic of diabetic vasculopathy, and that hyperpermeability in induced diabetic rats was largely prevented by infusion of soluble RAGE, the extracellular domain of the receptor, which blocks binding of AGEs to cell surface RAGE (page 238, col.2, first full paragraph).

As for the claim limitations concerning the choice of subject to be treated, the choice of fragment of the soluble receptor, the doses and methods of administration, they constitute obvious modifications for one of skill in the art.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eliane Lazar-Wesley, PhD, whose telephone number is (703) 305 4059. The examiner can normally be reached on Monday-Friday from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached on (703) 308-2731.

Official papers filed by fax should be directed to (703) 308 4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

ELW
September 29, 1998

LILA FEISEE
SUPERVISORY PATENT EXAMINER